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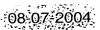
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CLAIMS

- 1. The use of a nucleic acid construct comprising a nucleic acid sequence encoding a member of the lipocalin protein family as a reporter gene for the detection of a gene activation event resulting from a change in or altered metabolic status in a cell in vitro or in vivo, wherein said cell is transfected with said construct.
- 2. The use as claimed in claim 1, in which the lipocalin protein is heterologous to the cell in which it is expressed.
- 3. A use as claimed in claim 1, in which the lipocalin protein is coded for by a nucleic acid construct comprising (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) a nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues
- 4. A use as claimed any one of claims 1 to 3, in which the lipocalin is selected from the group consisting of: ovine betalactoglobulin (BLG) (accession No. X12817), murine major urinary protein (MUP) (accession No. NM 031188) and rat α -2-urinary globulin (α -2u) (accession number M27434).
- 5. A use as claimed in claim 3 or claim 4, in which peptide sequence is an epitope.
- 6. A use as claimed in claim 5, in which the epitope is selected from the group consisting of EQKLISEEDL, GKPIPNPLLGLDST, YPYDVPDYA, NVRFSTIVRRRA, KQMSDRRENDMSPS, SGNEVSRAVLLPQSC, SSLSYTNPAVAATSANL, RSTLQHPDYLQEYST, VSTLLRWERFPGHRQA, KFQQLVQCLTEFHAALGAYV, QEQCQEVWRKRVISAFLKSP, and RLSDKTGPVAQEKS

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7. A use as claimed in any one of claims 2 to 6, in which the construct additionally comprises a promoter element upstream of the (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) and nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues.

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- 8. A use as claimed in claim 7, in which the promoter element may be selected from one of the following groups consisting of:
- (i) c-myc, p21/WAF-1, MDM2, Gadd45, FasL, GAHSP40, TRAIL-R2/DR5, BTG2/PC3;
 - (ii) MnSOD, CuZnSOD, IkB, ATF4, xanthine oxidase, COX2, iNOS, Ets-2, FasL/CD95L, yGCS, ORP150.

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(iii) Lrg-21, SOCS-2, SOCS-3, PAI-1, GBP28/adiponectin, α -1 acid glycoprotein, metallothioneine I, metallothioneine II, ATF3, IGFbp-3, VDGF and HIF1 α .

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- (iv) Gadd 34, GAHSP40, TRAIL-R2/DR5, c-fos, CHOP/Gadd153, APAF-1, Gadd45, BTG2/PC3, Peg3/Pwl, Siah1a, S29 ribosomal protein, FasL/CD95L, tissue tranglutaminase, GRP78, Nur77/NGFI-B, CyclophilinD, p73 and Bak.
- (v) a promoter from a xenobiotic metabolising cytochrome p450 enzymes from the 2A, 2B, 2C, 2D, 2E, 2S, 3A, 4A and 4B gene families.

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(vi) a synthetic promoter sequence comprised of a minimal eukaryote consensus promoter operatively linked to one or more response elements selected from the group consisting of the aryl hydrocarbon (Ah)/Ah nuclear translocator (ARNT) receptor response element, the antioxidant response element (ARE), the xenobiotic response element (XRE).

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- 9. A use as claimed in claim 1, in which the nucleic acid construct comprises a stress inducible promoter operatively isolated from a nucleic acid sequence encoding a member of the lipocalin protein family by a nucleotide sequence flanked by nucleic acid sequences recognised by a site specific recombinase, of by insertion such that it is inverted with respect to the transcription unit encoding a member of the lipocalin protein family, in which the construct additionally comprises a nucleic acid sequence comprising a tissue specific promoter operatively linked to a gene encoding the coding sequence for the site specific recombinase.
- 10. A use as claimed in claim 9, in which the site specific recombinase sequences are two loxP sites of bacteriophage P1.
 - 11. A use as claimed in any one of claims 1 to 10, in which the gene activation event is induction of toxicological stress, metabolic changes, or disease, including a disease that is the result of viral, bacterial, fungal or parasitic infection.
 - 12. A method of detecting a gene activation event in a cell in vitro or in vivo, comprising assaying a host cell stably transfected with a nucleic acid construct comprising a nucleic acid sequence encoding a member of the lipocalin protein family, or a transgenic non-human animal whose cells express such a construct, in which the cell or animal is subjected to a gene activation event that is signalled by expression of a peptide tagged lipocalin reporter gene.
 - 13. A method of screening for, or monitoring of toxicologically induced stress in a cell or a cell line or a non-human animal, comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct as defined in any one of claims 2 to 10.
- 14. A method for screening and characterising viral, bacterial, fungal, and parasitic infection comprising the use of a cell, cell line or non human animal which has been





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transfected with or carries a nucleic acid construct as defined any one of claims 2 to 10.

15. A method for screening for cancer, inflammatory disease, cardiovascular disease, metabolic disease, neurological disease and disease with a genetic basis comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct as defined in any one of claims 2 to 10.

